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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/278,601	07/21/1994	DAVID KNIPE	DFCI363A	6837

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EXAMINER

MOSHER, MARY

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/278,601

Applicant(s)

KNIPE ET AL.

Examiner

Mary E. Mosher, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/22/2004, 9/15/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-21, 31, 36, 41, 65, 68-73, 75-79, 83-97, 99-101, 104 and 109-148 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18-21, 31, 36, 41, 65, 68-73, 75-79, 83-97, 99-101 and 104 is/are allowed.
- 6) ☒ Claim(s) 109-148 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Continued Examination

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's second submission after final filed on 12/22/2004 has been entered. The supplemental amendment filed 9/15/2005 has been entered.

Response to Arguments

In response to applicant's arguments, the 102(b) rejection over Dobson et al is withdrawn. Applicants have argued that ICP4 mutation inhibits replication, but it does not render the virus replication defective. If an ICP4 mutation does not meet the claim limitations, then the rejection over Dobson is withdrawn.

In regard to interference papers 107 and 108, applicant argues the redeclaration of the count in paper 108 is clearly in error because it includes "or claim 49 of Knipe", which was not included in paper 107 in the discussion of what the count would be. However, the actual order (108) redeclaring the interference does include Knipe claims 35, 40, and 49 in the count, and this is the count which applicants conceded. It is noted that the same discussion in interference paper 107 refers to a nonexistent "Inglis '364" application; the examiner is of the opinion that typos are more likely to escape correction in a 99-page document (107) than in a 5-page one (108). In any case, the interference judge advised that a final judgment controls how applicant's claims are disposed, and the rejections below are based upon the final judgement in paper 133.

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Applicant further argued that there is no interference estoppel for new claims 109-148, because claim 49 of Knipe (actually parent claim 45) was directed to a virus "having **a mutation** in one or more genes encoding **a protein** essential for viral replication", and the terminology is directed to the case where a herpesvirus has duplicate genes of the same protein, for example ICP4. However, claim 49 stated "wherein the mutation is in the gene **or genes** encoding the proteins ICP8 or ICP27." Since ICP8 and ICP27 are encoded by unique genes, the use of plural "genes" in claim 49 cannot have referred to duplicate genes. Therefore this argument is unconvincing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

Claims 109-148 are rejected under 35 U.S.C. 102(g) as being unpatentable over the lost count of interference 104363.

To explain this rejection, here is the Knipe moiety of the final count, edited to read as independent claims:

(Knipe 49) A vaccine comprising a mutated HSV-1 or HSV-2 in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more of the gene or genes encoding the proteins ICP8 or ICP 27 to render the herpes replication

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defective, said mutated herpesvirus being present in an effective immunizing amount.

Or

(Knipe 35) A method of immunizing a mammal comprising administering to said mammal a vaccine comprising a mutated HSV-1 or HSV-2 capable of infecting a mammalian cell and of eliciting a protective immune response upon administration, said herpesvirus having a mutation in the gene or genes encoding the proteins ICP8 or ICP27 to render the herpesvirus replication defective.

Or

(Knipe 40) A method of inducing an immune response against herpesvirus in an mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus, said herpesvirus having a mutation in one or more of the gene or genes encoding the proteins ICP8 or ICP27 to render the herpesvirus replication defective.

The final ruling was that Knipe was not entitled to claim this subject matter.

Since the lost count refers to “a mutation in one or more genes” and “mutation in the gene or genes encoding the proteins ICP8 or ICP27”, the count clearly covered embodiments with mutation in ICP8, mutation in ICP27, and mutations in both ICP8 and ICP27. Since the lost count also uses the phrase “having a mutation”, the subject matter is open to additional, unspecified mutations. Therefore, claims 111-113, 121-123, 129-148 are drawn to the same invention as the lost count, and parent claims 109-110, 119-120 must also be rejected over the count. Claims 114-120, 124-123 specify two or more deletion mutations, and the count does not specify deletions; however, since deletions were widely known to be more stable than other types of mutations, this feature is not seen as sufficient to distinguish over the lost subject matter.

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Applicant may wish to consider if *In re Johnson and Farnham* (CCPA) 194 USPQ 187 suggests a workable approach. Stated broadly, applicants conceded priority to Inglis for the broad invention of immunogenic compositions & methods involving herpesviruses incapable of production of infectious new virus particles. Now applicants are pursuing a narrower invention, involving herpesviruses incapable of genome replication combined with an additional mutation. This narrower invention, though dominated by the Inglis claims, is not obvious over the Inglis disclosure, as Inglis provides at most a bare minimum of suggestion regarding mutations abolishing genome replication, and no particular motivation to choose such a mutation in combination with additional mutations. The complications arise because species claims to viruses with mutations in HSV ICP8, ICP27, and ICP8 + ICP27 were designated as corresponding to the count in the interference, and lost in the final judgment. The lost species claims were open to additional mutations, such as the unspecified second mutation now claimed.

Although it seems absurd that the interference with Inglis bars applicant from claiming HSV ICP8 and ICP27 mutants that are not taught or suggested by Inglis, that is the final judgment of the interference, which cannot be altered now by either the examiner or the applicant. Applicant has obviated judgments of unpatentability against many of the claims that were present in the interference, by amending the claims to their current form. Since subject matter broader than HSV ICP8 and ICP27 was concluded to be described and enabled in this application, applicant may wish to

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consider pursuing claims like 109, 110, 119, and 120 with a specific exclusion of HSV ICP8 and ICP27 (as in *Johnson*).

Allowable Subject Matter

Claims 18-21, 31, 36, 41, 65, 68-73, 75-79, 83-97, 99-101, 104 are allowed.

The following is a statement of reasons for the indication of allowable subject matter:

In the interference between Knipe (this application) and Inglis, claims involving the treatment of herpetic stromal keratitis were excluded from the interference. Therefore claim 18 and dependent claims are allowable.

Claims drawn to products and methods where the herpesvirus included a heterologous gene were excluded from the interference with Inglis. Although Inglis has another patent 6541009 with dominating claims to products and methods including heterologous genes, the Knipe claims are distinct from the Inglis claims. Knipe showed the ability to obtain an effective immune response to a heterologous gene using a herpesvirus unable to replicate the genome. This would not have been obvious to succeed based on the disclosure of Inglis; success would not have been reasonably expected given the reduced copy number and limited gene expression from genome-replication-defective herpesviruses. Also Inglis teaches a strong preference for using viruses defective in genes that are active only after genome replication. Therefore, claims 31, 36, 41, 68, 84, 91 and dependent claims are allowable and do not interfere with any Inglis patent.

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Also, the issue of potential interference with patents 5879934, 5658724, and 5804413 to DeLuca has been considered. At first glance, claims such as 68 and 104 would appear to interfere with claims such as claim 50 of patent 5,879,934 (DeLuca). Both parties claim priority to exactly the same date. A declaration of interference requires the claims to pass a two-way obviousness test. The vector of Deluca claim 50 would render obvious the composition of at least Knipe claims 68 and 104. Knipe teaches ICP27 as essential for viral genome replication and ICP4 as another mutation, so a prima facie case could be made that Deluca's claim is an obvious embodiment of Knipe's claim. However, Deluca teaches that the combination of ICP4 and ICP27 mutations solves a recognized problem of cytotoxicity in ICP4 mutants. Knipe does not contain any similar teaching, and does not provide any particular blazemarks to the ICP27 + ICP4 combination. Therefore, Deluca's disclosure of the solution to a long-standing problem is seen as a secondary consideration indicating nonobviousness, particularly in the absence of specific blazemarks to the combination in Knipe. Therefore, the claims of Knipe and Deluca do not pass the two-way obviousness test required for interference.

In regard to claims 65 and 104, neither the interference count nor the disclosure of Inglis point to the specific combination of deletion and nonsense mutations.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-


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272-0906. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

3/20/06


MARY E. MOSHER, PH.D.
PRIMARY EXAMINER